Resolution of choroidal metastasis in lung adenocarcinoma with gefitinib

Resolução de metástase coroidal em adenocarcinoma pulmonar com gefitinibe

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KEYWORDS:

Choroidal metastasis; Gefitinibe; Lung adenocarcinoma

ABSTRACT

The choroid is the structure with the highest occurrence of ocular metastasis. The sites that most commonly metastasize to the choroid are the lung and breast, with lung carcinoma responsible for about 30% of choroidal metastases. We report a case of a female patient with choroidal metastasis in the left eye due to pulmonary adenocarcinoma. The patient presented low visual acuity with the presence of a mass in the upper temporal region, endophytic, irregular and non-pigmented, associated with a detachment of sensorineural retina. It was conducted with the immunomodulator Gefitinib, a drug class of tyrosine kinase inhibitors. After 03 months using the medication, the patient showed improvement in visual symptoms, and marked regression of the lesion in the left eye. The result shows the benefit of this medication in a patient with this specific type of tumor.

PALAVRAS-CHAVE:

Metástase coroidal; Gefitinibe; Adenocarcinoma pulmonar

RESUMO

A coroide é a estrutura de maior ocorrência de metástase ocular. Os sítios que mais comumente metastatizam para a coroide são o pulmão e mama, sendo o carcinoma pulmonar responsável por cerca de 30% das metástases coroidais. Relatamos o caso de uma paciente do sexo feminino com metástase coroidal em olho esquerdo por adenocarcinoma pulmonar. A paciente apresentou baixa da acuidade visual com a presença de massa em região temporal superior, endofítica, irregular e não-pigmentada, associada a um descolamento de retina neurossensorial. Foi conduzida com o imunomodulador Gefitinibe, um medicamento classe dos inibidores da tirosina quinase. Após 03 meses em uso da medicação, a paciente apresentou melhora dos sintomas visuais, e acentuada regressão da lesão em olho esquerdo. O tratamento evidencia o benefício da medicação em paciente com este tipo específico de tumor.

INTRODUCTION

The choroid is the most frequent ocular site of metastases occurrence[1], and other sites include the ciliary body, the iris, the neural retina, the optic nerve, and, in some cases, the vitreous[2]. In addition, only 25% of such cases are identified as the primary tumor site at diagnosis[2].

The most common sites for cancers to metastasize to the choroid include the lung and breast[1,3], with lung carcinoma accounting for approximately 30% of choroidal metastases. Symptoms such as blurred vision, visual field loss and/or decreased visual acuity are the most frequent visual symptoms[2,3] and are typically some of the first symptoms to appear.

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In addition to the more frequent occurrence of ocular metastasis in patients with adenocarcinoma, high serum levels of biomarkers-carcinoembryonic antigen (CEA), cancer antigen 15-3 (CA15-3), and total prostate-specific antigen (PSA)-would have a positive predictive value for ocular metastasis in older adults[4].

In Brazil, approximately 70% of cases present with locally advanced or metastatic disease at the time of diagnosis[5]. Although lung cancer represents the main cause of mortality among neoplasms[6,7], two-thirds of secondary choroidal metastases show favorable responses to different systemic or ocular treatments, promoting early diagnosis and treatment and consequently increasing the patient's quality of life.

Systemic chemotherapy is more effective in the treatment of ocular metastases, especially in chemosensitive tumors, such as small-cell carcinoma[2]. Regarding cases of non-small-cell neoplasia, several case reports have reported the reversal of choroidal metastasis through the administration of bevacizumab, an anti-vascular endothelial growth factor (anti-VEGF)[8-10]. Chemotherapy, photocoagulation, cryosurgery, and surgical resection are among the options currently available for ocular metastases[2].

The occurrence of ocular metastasis is higher in patients with advanced disease and in cases of adenocarcinoma; histological type that became the most frequent in the last 15 years[2]. These two characteristics associated with the improvement in survival obtained from the new therapeutic modalities, targeted molecular therapy, and immunotherapy[11], suggest that newly diagnosed patients could benefit from a routine screening for ocular metastasis.

Gefitinib is a selective inhibitor of epidermal growth factor receptor (EGFR) tyrosine kinase, which is commonly expressed in human solid tumors of epithelial origin. Inhibition of EGFR tyrosine kinase activity inhibits tumor growth, metastasis and angiogenesis, increasing apoptosis of tumor cells[12].

The objective of this report is to present a case where a choroidal metastasis associated with lung adenocarcinoma was resolved with the use of systemic gefitinib.

CASE REPORT

A 60-year-old female patient, asymptomatic, during routine chest X-ray examinations, a mass in her left lower lobe of the lung (LLL) was observed. The patient had no comorbidities and denied smoking. The positron emission tomography–computed tomography (PET-CT) performed in the sequence showed a pulmonary mass measuring 5.0 × 4.0 × 3.5 cm in the LLL and mediastinal lymph nodes in subcarinal, inferior and bilateral paratracheal chains, in the left inferior pulmonary ligament and descending thoracic aortic and lymph node in the left pulmonary hilum. She underwent LLL lobectomy and drainage of mediastinal lymph nodes in another service.

Pathological examination revealed lung adenocarcinoma (NSCLC), pathological staging pT2b pN2. The search for EGFR mutation (activating mutation of epidermal growth factor receptor) was positive for exon 19 deletion and lack mutations in KRAS, NRAS, BRAF, and ALK genes. For PDL-1 search, an expression of 30% was observed.

After surgery, the patient was referred to the Oncopneumology Service of HC Unicamp for adjuvant treatment (4 cycles of carboplatin+paclitaxel and sequential radiotherapy in mediastinum 4500 cGy 3D). PET-CT post chemotherapy showed ground-glass opacities and interlobular interstitial thickening in the left upper lobe (LUL), corresponding to post-radiotherapy pneumonitis.

One year after the end of chemotherapy, she presented with the recurrence of a hyper-captivating pulmonary mass in the middle lobe. The patient experienced holocranial headache and blurred vision, associated with photopsias. Cranial tomography showed no alterations; however, retinal mapping showed a subretinal macular lesion with whitish appearance, elevated with approximately 10 papillary diameters of the superior temporal region. Visual acuity in the right eye of 20/20, without significant injuries; and visual acuity of 20/50 in the left eye, associated with a solid, endophytic lesion, with irregular, hypochromic, delimitation in the superior temporal region measuring approximately 10 mm at the base on retinography and height of 2.8 mm on ultrasound, with the presence of inferior sectoral serous retinal detachment and absence of Kappa angle. Optical coherence tomography (OCT) showed sensorineural retinal detachment, with perifoveal involvement and choroidal bulging in the superior temporal region, with compression of the external retina (Figure 1).

Owing to the progression of metastatic disease, gefitinib 250 mg/day was introduced. After 03 months using gefitinib 250 mg, the patient had improvement in visual symptoms, recovery of visual acuity

to 20/20 and marked regression of the left eye lesion, with superior temporal focal alteration of the retinal pigment epithelium, without signs of activity, with OCT of the lesion area showing atrophy of the cystic spaces of the Satler and Haller layers, but maintenance of the integrity of the outer and inner retinal layers and the ellipsoid zone. In a new PET-CT the disease remission was observed, with no metastatic lesions and no signs of active disease (Figures 2 a 5)

DISCUSSION

Systemic medications circulate freely through the choroid, not being involved in the blood-retinal barrier, owing to the choroidal capillaries, but the effectiveness of chemotherapeutic agents depends on tumor susceptibility[8]. The prompt response to metastatic control, with a single treatment using gefitinib, for patients with EGFR mutation has shown excellent and surprising responses[13].

Figure 1. Optical coherence tomography (OCT) on A-scan (left) shows a heterogeneous reflectance mass with irregular margins, demonstrating on B-scan (right) an elevation with irregular edges in choroidal topography with adjacent subretinal fluid in the superior temporal arcade. A disorganization of the outer layers with hyperreflective points was observed.
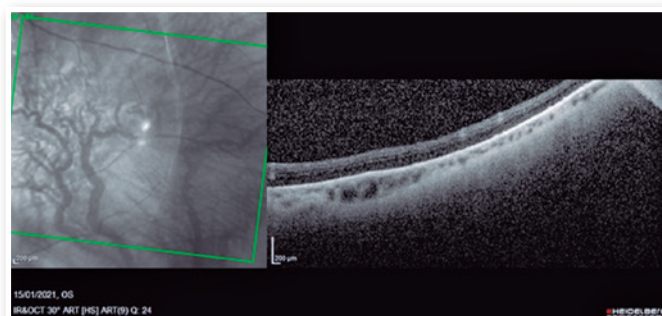
Figure 2. Optical coherence tomography (OCT) in the A-scan image (on the left) reveals presence of two large vascular branches, suggesting that they are the vessels supplying the metastasis. The B-scan image (on the right) shows increased thickness of the choroid in the region where the tumor was located, in addition to the absence of external layers.
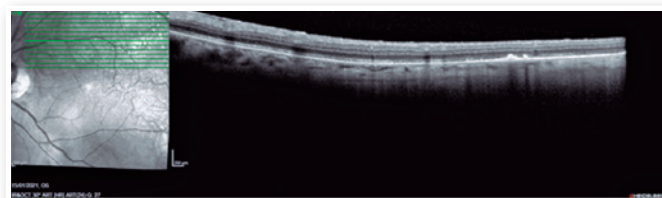
Figure 3. OCT in the B-scan we can note an accumulation of subretinal hyperreflective material and attenuation of the ellipsoid layer.

Figure 4. PET-CT scan demonstrating an area of hypermetabolism in the left humerus (SUV = 8.5), suggestive of metastasis.
*SUV (standard uptake value), which expresses the metabolic activity of this lesion
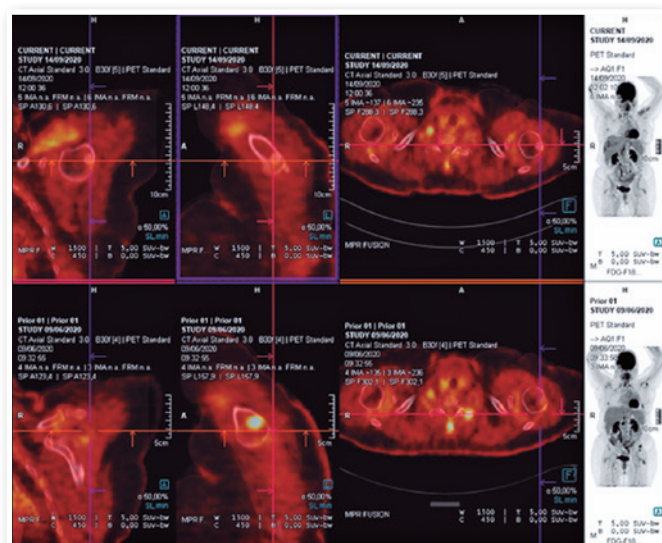
Figure 5. PET-CT scan demonstrating regression of the lesion in the left humerus after gefitinib therapy.

In the present case, we demonstrated a complete remission of ocular metastasis in a patient with EGFR mutation exon 19 deletion, resulting in excellent quality of life. Recent studies have shown that gefitinib prolongs disease-free survival, preserving a favorable quality of life[13,14].

Female patients or of Asian ethnicity who have never smoked, with adenocarcinoma histology, are more likely to benefit from gefitinib treatment[13]. These clinical features are also associated with high rates of EGFR[13] mutation-positive tumors and are those found in the reported case.

Other treatment options for ocular choroidal metastases described in the literature include external beam radiotherapy, brachytherapy, laser, and photodynamic therapy[15].

In conclusion, in this case report, we demonstrated the surprising effectiveness in resolving choroidal metastasis of lung adenocarcinoma in a patient with EGFR mutation. We believe that to avoid irreversible impairment or visual loss, screening tests should be performed early, in cases of breast and lung cancer for the early diagnosis and treatment of ocular metastases.

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